
Glucose inhibits cardiac muscle maturation through nucleotide biosynthesis.

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Authors: Haruko Nakano, Itsunari Minami, Daniel Braas, Herman Pappoe, Xiuju Wu, Addelynn Sagadevan, Laurent Vergnes, Kai Fu, Marco Morselli, Christopher Dunham, Xueqin Ding, Adam Z Stieg, James K Gimzewski, Matteo Pellegrini, Peter M Clark, Karen Reue, Aldons J Lusis, Bernard Ribalet, Siavash K Kurdistani, Heather Christofk, Norio Nakatsuji, Atsushi Nakano

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Public Summary:

Genetically-inherited heart disease is common in babies born to Mother's with high blood glucose levels during pregnancy (Gestational diabetes). Using an induced stem cell model of heart cell maturation from stem cells to functional beating heart cells, we tested high glucose levels on these cells in culture. Our data suggest that gestational diabetes late in pregnancy suppresses heart maturation, providing a possible reason for why heart disease occurs in the offspring from a diabetic pregnancy.

Scientific Abstract:

The heart switches its energy substrate from glucose to fatty acids at birth, and maternal hyperglycemia is associated with congenital heart disease. However, little is known about how blood glucose impacts heart formation. Using a chemically defined human pluripotent stem-cell-derived cardiomyocyte differentiation system, we found that high glucose inhibits the maturation of cardiomyocytes at genetic, structural, metabolic, electrophysiological, and biomechanical levels by promoting nucleotide biosynthesis through the pentose phosphate pathway. Blood glucose level in embryos is stable in utero during normal pregnancy, but glucose uptake by fetal cardiac tissue is drastically reduced in late gestational stages. In a murine model of diabetic pregnancy, fetal hearts showed cardiomyopathy with increased mitotic activity and decreased maturity. These data suggest that high glucose suppresses cardiac maturation, providing a possible mechanistic basis for congenital heart disease in diabetic pregnancy.

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